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Stereotactic Radiosurgery-Induced Peritumoral Edema in Asymptomatic Convexity, Parasagittal, and Parafalcine Meningiomas

Osman Burak CAN[1], Mete RUKSEN[2], Burcu DURMAK ISMAN[1], Mehmet Orbay ASKEROGLU[1], Seray ZORLU[3], Alper YUKSEL[3], Dilsat CAMLI[3], Ali AKAY[4]

[1]Acibadem Kent Hospital, Department of Radiation Oncology, Izmir, Türkiye
[2]Acibadem Kent Hospital, Department of Neurosurgery, Izmir, Türkiye
[3]Acibadem Kent Hospital, Department of Radiology, Izmir, Türkiye
[4]Izmir University of Economics, Medical Point Hospital, Department of Neurosurgery, Izmir, Türkiye

Corresponding author: Osman Burak CAN ✉ osmanburakcan@gmail.com

ABSTRACT

AIM: To evaluate the incidence and identify the risk factors of stereotactic radiosurgery (SRS)-induced peritumoral edema (PTE) in the asymptomatic convexity, parasagittal, and parafalcine meningiomas without pre-existing PTE.

MATERIAL and METHODS: We retrospectively analyzed 52 patients with asymptomatic convexity, parasagittal, or parafalcine meningiomas without pre-existing PTE who underwent single-fraction Gamma Knife radiosurgery between 2019 and 2024. The median tumor volume and the maximum tumor diameter were 3.3 cc (range: 0.31–10.2 cc) and 2.0 cm (range: 0.98–3.1 cm), respectively. The median margin dose was 12 Gy (range: 11 Gy–13 Gy). The median radiological and clinical follow-up durations were 21 months (range: 6–65 months) and 26 months (range: 12–66 months), respectively.

RESULTS: SRS-induced PTE occurred in 5.8% of patients (n=3), exclusively in elderly individuals (≥65 years) with parasagittal or parafalcine meningiomas. No cases were observed in convexity meningiomas (0/24). Multivariable analysis revealed a trend toward statistical significance for the association between age and SRS-induced PTE (p=0.074). In the overall cohort, the incidence of SRS-induced PTE was significantly higher in elderly patients compared to younger patients (<65 years) (3/14 vs. 0/38, p=0.016), and this difference remained significant within the parasagittal/parafalcine subgroup (3/7 vs. 0/21, p=0.011).

CONCLUSION: SRS appears to be a safe treatment modality in terms of PTE risk in patients aged below 65 years with asymptomatic convexity, parasagittal, or parafalcine meningiomas without pre-existing PTE. In contrast, elderly patients with parasagittal or parafalcine meningiomas may be more susceptible to SRS-induced PTE, thereby warranting a more cautious approach to SRS in this subgroup. Additional studies involving larger cohorts are warranted to validate these findings.

KEYWORDS: Stereotactic radiosurgery, Meningioma, Brain edema

ABBREVIATIONS: SRS: Stereotactic radiosurgery, **PTE:** Peritumoral edema, **RANO:** Response Assessment in Neuro-Oncology

Osman Burak CAN : 0000-0001-5184-8990
Mete RUKSEN : 0000-0002-0521-8143
Burcu DURMAK ISMAN : 0009-0000-4515-2444
Mehmet Orbay ASKEROGLU : 0000-0001-7126-6373
Seray ZORLU : 0000-0002-0912-3264
Alper YUKSEL : 0009-0006-7436-4749
Dilsat CAMLI : 0009-0001-0225-3306
Ali AKAY : 0000-0002-7187-398X

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INTRODUCTION

Meningiomas are the most common benign brain tumors (21). The detection of incidental meningiomas has increased in recent years due to the rising use and widespread availability of brain magnetic resonance imaging (MRI) (30). Consensus guidelines recommend active surveillance to avoid treatment-related complications in patients with asymptomatic meningiomas (5,11). However, delaying treatment until symptoms emerge could result in inevitable surgical intervention or neurological deficits. In a retrospective analysis, Kim et al. reported that approximately two-thirds of patients with asymptomatic meningiomas exhibited tumor growth, and one-third eventually requiring surgical intervention during follow-up (14). In addition, a prospective study that assessed the growth rate of incidental meningiomas revealed that 75% of tumors demonstrated a volume increase of over 15% over a mean duration of 2.2 years (1). Additionally, tumors that grow during surveillance may fall outside the window of opportunity for stereotactic radiosurgery (SRS). Moreover, prolonging follow-up times can lead to patient anxiety, referred to as "scanxiety" (2). Consequently, the optimal management strategy for incidental meningiomas remains a subject of ongoing debate.

The question of whether performing SRS constitutes overtreatment in the management of incidental meningiomas remains controversial; however, SRS has been shown to be both safe and effective for treating these tumors. A recent international multicenter study, the Incidental Meningioma Progression During Active Surveillance or After Stereotactic Radiosurgery (IMPASSE), demonstrated that SRS provides superior radiological tumor control compared to the observation of incidental meningiomas (26). This enhanced tumor control was achieved without an increased risk of neurological deficits. The IMPASSE study provides a new perspective on the management of asymptomatic meningiomas.

Although SRS is an effective treatment option, it carries the potential risk of inducing or exacerbating peritumoral edema (PTE). This represents the most common complication of SRS for non-skull-base meningiomas. The reported incidence of SRS-induced PTE in patients with meningioma ranged from 15.3% to 38.2% (3,4,7,8,15,19,20,27). While most cases were asymptomatic, 5% to 15.1% of patients experienced new or worsening neurological symptoms, including headache, seizures, or focal deficits due to edema. Although a majority of these symptoms resolve with corticosteroid treatment, 1%–5.2% of patients may suffer progressive symptoms, with a few patients requiring surgical intervention (15,23,27).

Further, several studies have revealed that convexity, parafalcine, and, in particular, parasagittal meningiomas are associated with an increased risk of SRS-induced PTE or radiation-related complications compared to skull-base meningiomas (23,24,27). Additionally, pre-existing PTE has been identified as a strong predictor of SRS-induced PTE (3,8,17). Therefore, in our clinical practice, treatment with SRS for asymptomatic meningiomas located in high-risk regions such as the convexity, parasagittal, and parafalcine areas is usually avoided if PTE is present. However, the safety of SRS in terms of the development of PTE for incidental meningiomas that lack pre-existing PTE and are located in high-risk regions remains unclear. Therefore, in this retrospective study, our objective is to assess the incidence and factors associated with SRS-induced PTE in asymptomatic convexity, parasagittal, and parafalcine meningiomas without PTE at the time of diagnosis.

MATERIAL and METHODS

Patients

This study included patients diagnosed with incidental and asymptomatic meningiomas located in the cerebral convexity, parasagittal, or parafalcine locations, with no evidence of PTE prior to SRS and a clinical follow-up period of at least 12 months. Patients with biopsy-confirmed World Health Organization (WHO) grades 2 or 3 meningiomas as well as those with a history of prior radiotherapy or surgery were excluded. "Asymptomatic" was defined as the absence of any symptoms or signs attributable to the tumor's specific location (8). Between 2019 and 2024, 224 patients with meningioma underwent Gamma Knife radiosurgery at our institution, of whom 52 met the inclusion criteria and were enrolled in this study.

Ethical approval for this retrospective study was obtained from the local ethics committee (ATADEK; Decision No: 2024-10/379, Date: 18.07.2024). Informed consent was obtained from all patients.

Treatment Decision Process

Treatment decisions were made after informing patients of the available options, including surgery, SRS, or active surveillance. A thorough discussion of the potential risks, benefits, and side effects of each option was conducted with each patient, and informed consent from the patients was obtained prior to SRS.

Radiosurgery Technique

All patients underwent single-fraction SRS using the Gamma Knife Perfexion system (Elekta AB, Stockholm, Sweden). A Leksell stereotactic frame was applied under local anesthesia. Following frame placement, stereotactic MRI was performed, obtaining post-contrast T1-weighted MPR sequence images with a slice thickness of 1 mm. Treatment planning was collaboratively conducted by a neurosurgeon and a radiation oncologist. The median margin dose was 12 Gy (range: 11 Gy–13 Gy), with a mean margin dose of 12.1 Gy. The median isodose line was 50% (range: 45%–55%). Radiosurgery parameters are detailed in Table I.

Follow-Up

Post-SRS follow-up included a contrast-enhanced brain MRI at six months, followed by annual imaging thereafter. Following treatment, clinical evaluations were recommended twice annually to assess the neurological status and identify any potential complications.

The Primary Objective: SRS-Induced PTE

The primary objective of this study was to determine the incidence and to identify the risk factors for SRS-induced PTE, defined as the newly developed peritumoral T2 hyperintensity

Table I: Radiosurgery Parameters

Radiosurgery Parameters	Median (range)
Margin Dose (Gy)	12 (11–13)*
Maximum Tumor Dose (Gy)	24 (22–26.7)
Mean Tumor Dose (Gy)	16.9 (14.9–19.6)
Prescribed Isodose Line (%)	50 (45–55)
Tumor Coverage (%)	99 (98–100)
Gradient Index	2.83 (2.53–3.20)
Selectivity	0.86 (0.77–0.96)
Number of Shots	22 (4–75)

**Among the total cohort of 52 patients, a margin dose of 11 Gy was administered to 4 patients, 12 Gy to 39 patients, and 13 Gy to 9 patients.*

observed on MRI in the absence of tumor progression. Symptomatic edema was defined as the presence of edema-related symptoms that required corticosteroid therapy.

Tumor Response

Tumor responses were evaluated according to the Response Assessment in Neuro-Oncology (RANO) criteria for meningiomas, based on the sum of the products of perpendicular diameters of all target lesions. Partial response was defined as a decrease of ≥50%, minor response as a decrease of ≥25% but <50%, progressive disease as an increase of ≥25%, and stable disease as changes not meeting the criteria for other categories, with all changes sustained for at least eight weeks or until the next scheduled scan, whichever was longer (9).

Statistical Analysis

Chi-Square (χ^2) test or Fisher's exact test was performed for categorical variables, while the Mann–Whitney U test was applied for continuous variables. The Kruskal–Wallis test was employed to assess differences between groups based on tumor location. Variables included in the multivariable model were selected based on their statistical significance in the univariable analysis and/or their established relevance to PTE in previous studies, such as tumor location and volume. Due to the relatively small sample size and the low event rate of SRS-induced PTE, a post hoc power analysis was performed to assess the robustness of statistically significant findings.

RESULTS

The median patient age was 55 years (range: 34–76 years). Among the 52 patients, 8 (15.4%) were male, and 44 (84.6%) were female. SRS was performed in 14 patients (26.9%) due to tumor progression detected during active surveillance, while the remaining 38 patients (73.1%) underwent SRS immediately after diagnosis. The median tumor volume was 3.3 cc (range: 0.31–10.2 cc), and the median maximum tumor diameter was 2.0 cm (range: 0.98–3.1 cm). The median clinical follow-up duration was 26 months (range: 12–66 months), while the median radiological follow-up duration was 21 months (range: 6–65 months). A median of two MRI scans (range: 1–5) were performed after SRS.

Local tumor control was achieved in 100% of cases. According to the RANO criteria, 7 patients (13.5%) exhibited a partial response, 6 patients (11.5%) exhibited a minor response, and the remaining 39 patients (75%) had stable disease. There were no significant differences in age, gender, tumor volume, maximum tumor diameter, margin dose, or follow-up durations among patients with convexity, parafalcine, and parasagittal meningiomas (Table II).

Among the 52 patients, one patient (1.9%) with a parasagittal meningioma developed symptomatic PTE and two patients (3.8%) with a parafalcine meningioma developed asymptomatic PTE. Notably, no cases of PTE were observed in convexity meningiomas (0/24). Overall, SRS-induced PTE (both asymptomatic and symptomatic) occurred in 5.8% of patients. No additional late-onset complications related to SRS were observed. A moderately positive and statistically significant association was observed between age and tumor volume (ρ=0.495, p<0.001). The univariable analysis revealed a significant association between age and SRS-induced PTE (p=0.026). The multivariable model demonstrated a good overall fit (McFadden's R^2 = 0.632), and age revealed a trend toward statistical significance (p=0.074). Moreover, SRS-induced PTE was detected in 3 out of 14 elderly patients (≥ 65 years), whereas no cases were observed in younger patients (<65 years; 0/38), with this difference being statistically significant (p=0.016). In addition, no significant association was found between SRS-induced PTE and gender, maximum tumor diameter, tumor volume, margin dose, or tumor location. Comorbidities such as diabetes mellitus and hypertension were also not found to be associated with the development of SRS-induced PTE (Table III).

In the overall cohort, since SRS-induced PTE was exclusively observed in patients with parasagittal/parafalcine meningiomas, these 28 patients were analyzed separately, excluding those with convexity meningiomas. SRS-induced PTE was found to be significantly more frequent in elderly patients compared to younger patients with parasagittal/parafalcine meningiomas (3/7 vs. 0/21, p=0.011).

Although the observed differences were statistically significant for age in the univariable analysis and in comparisons between elderly and younger patients—both in the overall cohort and among those with parasagittal/parafalcine meningiomas—the post hoc statistical power of these analyses was <80%.

DISCUSSION

SRS-induced symptomatic PTE typically manifests among patients between three- and nine-months post-treatment, with its cumulative incidence increasing until 12 months and subsequently resolving within 2 years following SRS (8,29). Based on this timeframe, we included only patients with a clinical follow-up period of at least 12 months in this study. The median radiological and clinical follow-up durations were

Table II: Patient, Tumor, and Treatment Characteristics and the Incidence of PTE

	Entire Cohort n=52	Convexity n=24	Parafalcine n=17	Parasagittal n=11	p-value*
Age, Median (range) (years)	55 (34–76)	59 (34–71)	51 (36–76)	47 (34–70)	0.275
Gender					0.795
Male, n (%)	8 (15.4)	4 (16.7)	3 (17.6)	1 (9)	
Female, n (%)	44 (84.6)	20 (83.3)	14 (82.4)	10 (91)	
Tumor diameter (max), median, range (cm)	2.0 (0.98–3.1)	1.75 (1–3)	2.1 (0.98–3.1)	2.3 (1.4–2.9)	0.164
Tumor volume, median, range (ml)	3.3 (0.31–10.2)	2.25 (0.31–10.1)	4.1 (0.5–10.2)	4.3 (1.23–8.4)	0.444
Timing of SRS					0.924
Following tumor progression, n (%)	14 (26.9)	7 (29.2)	4 (23.5)	3 (27.3)	
Immediately after diagnosis, n (%)	38 (73.1)	17 (70.8)	13 (76.5)	8 (72.7)	
Margin dose	12 Gy (11 Gy–13 Gy)	12 Gy (11 Gy–13 Gy)	12 Gy (11 Gy–13 Gy)	12 Gy (11 Gy–13 Gy)	0.683
Follow-up (months)					
Clinical, median, (range)	26 (12–66)	24.5 (13–59)	32 (12–66)	26.5 (13–54)	0.714
Radiological, median, (range)	21 (6–65)	24 (7-48)	29 (6-65)	14.5 (6-35)	0.139
SRS-induced symptomatic PTE, n (%)	1 (1.9)	0 (0.0)	0 (0.0)	1 (9.0)	0.155
SRS-induced asymptomatic PTE, n (%)	2 (3.8)	0 (0.0)	2 (11.8)	0 (0.0)	0.122
SRS-induced symptomatic or asymptomatic PTE, n (%)	3 (5.8)	0 (0.0)	2 (11.8)	1 (9.0)	0.251

Statistical differences among the convexity, parasagittal, and parafalcine groups.* ***SRS:* *Stereotactic radiosurgery.* ***PTE:*** *Peritumoral edema.*

Table III: Risk factors for SRS-induced PTE (n=52)

Factors	Univariable Analysis	Multivariable Analysis
	p-value	
Age	**0.026**	0.074
≥65 vs. <65	**0.016**	-
Gender		
Male vs. Female	0.447	-
Tumor Diameter (maximum)	0.145	-
Tumor Volume	0.272	0.153
Margin Dose	0.407	-
Tumor Location	0.208	0.997
Convexity vs. Parafalcine	0.166	-
Convexity vs. Parasagittal	0.314	-
Convexity vs. Parafalcine/Parasagittal	0.240	-
Parasagittal vs. Parafalcine	0.823	-
Hypertension	0.546	-
Diabetes Mellitus	0.553	-

SRS: *Stereotactic radiosurgery.* ***PTE:*** *Peritumoral edema.*

21 and 26 months, respectively, which were deemed sufficient to assess SRS-induced PTE (3,17,29). Although the follow-up durations were not sufficient to reliably evaluate tumor control or response rates, these data were descriptively presented to provide a comprehensive overview of post-SRS outcomes. However, it should be emphasized that the primary focus of this study was the evaluation of SRS-induced PTE.

While asymptomatic PTE is primarily a radiological finding, symptomatic PTE is of greater clinical significance because it necessitates medical or surgical intervention. In our cohort, only one patient (1.9%) developed symptomatic PTE following SRS. At four months post-SRS, this patient presented with headaches and seizures, which were successfully managed with antiepileptic and corticosteroid therapy, thereby resulting in complete symptom resolution (Figures 1 and 2). In two patients (3.8%) with SRS-induced asymptomatic PTE, the edema did not require intervention and spontaneously resolved during follow-up.

Although a moderate positive correlation between age and tumor volume was observed in this study, this finding may be influenced by our clinical approach to managing meningiomas in elderly patients. In our clinical practice, small-volume meningiomas in elderly patients are more likely to be managed with surveillance rather than immediate intervention.

It is noteworthy that SRS-induced PTE was not observed in any of the 38 patients (0%) aged below 65 years, whereas it occurred in 3 out of 14 elderly patients (21.4%). Sheehan et al. identified meningiomas located in the parasagittal/parafalcine regions as being at higher risk for developing SRS-induced PTE, likely due to tumor abutment or the invasion of venous sinuses or other vascular structures (27). Although our study did not demonstrate a statistically significant difference in the

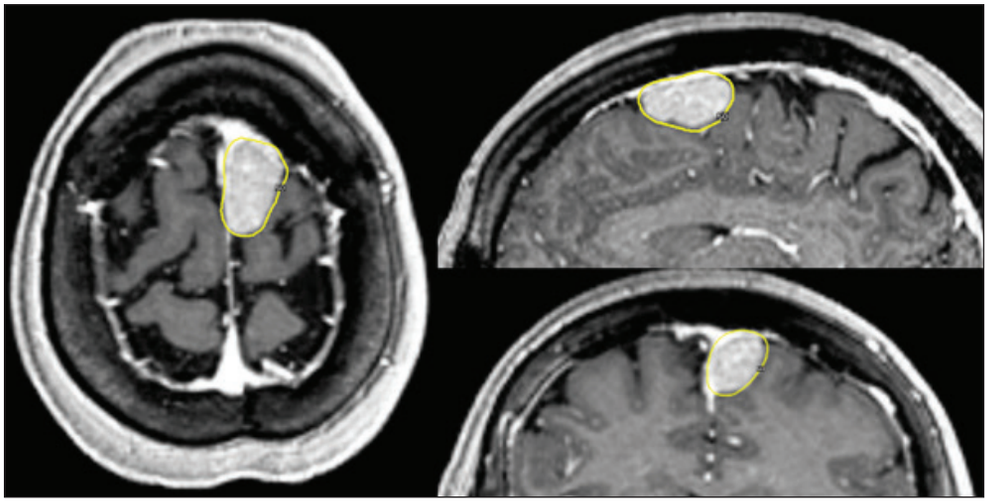

Figure 1: Axial, sagittal, and coronal post-contrast T1W MRI images show an asymptomatic parasagittal meningioma (tumor volume: 4.2 ml) in a 68-year-old female patient. The prescribed Gamma Knife treatment plan was a dose of 12 Gy to the 50% isodose line (yellow contours).

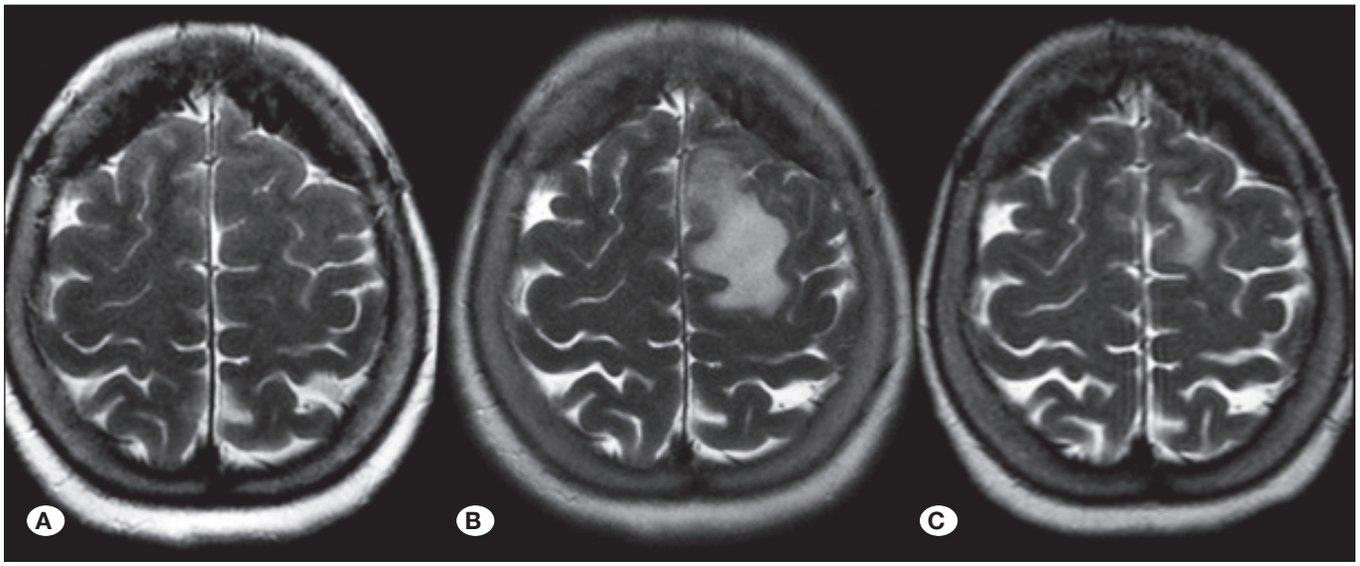

Figure 2: T2W axial MRI images obtained before Gamma Knife treatment **(A)**, post-treatment at 4 months **(B)**, and at 11 months **(C)**.

incidence of SRS-induced PTE between parasagittal/parafalcine and convexity meningiomas—possibly due to the small sample size or limited number of events—all three cases of SRS-induced PTE in our cohort occurred in elderly patients with parasagittal or parafalcine meningiomas. In line with our findings and those of previous studies, when the analysis was restricted to parasagittal/parafalcine meningiomas, we found that 42.9% (3/7) of elderly patients developed PTE, while none (0/21) of the younger patients did.

While the limited number of SRS-induced PTE cases and small sample size may constrain the statistical power to establish a definitive association between age (or elderly status) and the development of SRS-induced PTE, the complete absence of edema among younger patients remains a key observation in our study.

Thus, these findings suggest that SRS may represent a safe treatment modality with respect to SRS-induced PTE development in patients below 65 years of age and presenting with asymptomatic convexity, parasagittal, or parafalcine meningiomas without pre-existing edema, as no cases were observed in this group. In contrast, elderly patients with parasagittal or parafalcine tumors may be at increased risk of developing SRS-induced PTE. Therefore, the indication for SRS in this subgroup should be approached with caution and further evaluated in larger cohorts.

Several studies have investigated factors associated with the risk of SRS-induced PTE. Well-established risk factors include larger initial tumor volume, higher margin dose, pre-existing PTE, and non-skull-base tumor location. Additionally, venous sinus invasion and a large tumor–brain contact interface area have been identified as significant predictors of SRS-induced PTE (15,17). In a few studies, increased age has also been associated with SRS-induced PTE (3,15). In a study evaluating 331 patients with meningioma treated with SRS, PTE was observed in 15.4% of cases, and Kollová et al. reported that age over 60 years was a significant risk factor for the development of edema (15). Although the age threshold in our study was slightly higher (≥65 years), our findings support the previously reported association between increasing age and a higher risk of SRS-induced PTE.

Mechanism of SRS-Induced PTE

PTE in meningiomas is predominantly vasogenic, a phenomenon attributed to SRS-induced increases in capillary permeability, which subsequently leads to enhanced edema formation (21). Elevated levels of vascular endothelial growth factor (VEGF) have also been implicated in this process (13,22). Moreover, Cai et al. proposed that SRS-induced damage to the arachnoid membrane and pia mater at the tumor–brain interface significantly contribute to the development of PTE (3).

Tumor Location

Several studies have examined the correlation between tumor location and SRS-induced PTE in meningiomas (4,17,23). Although skull-base meningiomas may present long-term complications, such as cranial nerve deficits, SRS-induced PTE is relatively uncommon in these tumors. In contrast, meningiomas located in the convexity, parasagittal, and parafalcine locations—often referred to as cerebral hemispheric meningiomas—demonstrate a higher incidence of SRS-induced PTE compared to skull-base meningiomas. Chang et al. reported a 21.2% rate of symptomatic imaging changes in MRIs for cerebral hemispheric meningiomas and a 40% rate for parasagittal meningiomas, whereas skull-base meningiomas had a significantly lower incidence of 1.3% (4).

In a multicenter retrospective study, Sheehan et al. examined the risk factors for post-SRS PTE, specifically in parasagittal and parafalcine meningiomas. At a median dose of 14 Gy, new or worsening edema was observed in 38.2% of cases, and 5.2% of patients experienced progressive edema. Furthermore, 15.1% and 2.4% of patients required steroids or bevacizumab, respectively, while 7.1% underwent surgery due to edema. The patient population in their study may have been more susceptible to edema development because it included grades 2 and 3 meningiomas, which necessitate higher margin doses. Additionally, neurological deficits or symptoms were common prior to SRS, with 45.3% of patients exhibiting pre-existing PTE. In our study, SRS-induced PTE developed in 3 out of 28 (10.7%) parasagittal/parafalcine meningiomas; notably, all patients were asymptomatic at diagnosis and had no pre-existing PTE prior to treatment (27).

In another study, Cai et al. reported that among 105 meningiomas without pre-existing PTE, 16.19% of the patients developed edema following SRS. They also identified the tumor–brain contact interface area as one of the most significant risk factors for post-SRS PTE; specifically, for each increase of 1 cm^2 in the interface area, the likelihood of developing edema increased by 26% (3). Furthermore, some studies have indicated that parasagittal locations are particularly susceptible to PTE following SRS (17,23). Patil et al. demonstrated that the risk of post-SRS symptomatic edema was four times higher in parasagittal meningiomas compared to non-midline supratentorial meningiomas, with symptomatic edema occurring in 35.2% of parasagittal meningiomas versus 7.8% of non-parasagittal supratentorial meningiomas (23).

In our study, although we were unable to establish a correlation between tumor location and SRS-induced PTE, the absence of SRS-induced PTE in all 21 patients with parasagittal/parafalcine meningiomas aged below 65 years and in all 24 patients with convexity meningiomas is a noteworthy finding that may provide supportive evidence for the safety of SRS in these subgroups.

Pre-Existing PTE

Pre-existing PTE is a critical predictor of the risk of SRS-induced PTE (3,8,17). Cai et al. demonstrated that the risk of SRS-induced PTE is six times higher in meningiomas with pretreatment edema than in those without (3). Similarly, Hoe et al. found that the presence of PTE prior to SRS is significantly associated with an increased risk of developing SRS-induced PTE, even in asymptomatic meningiomas (8). Consequently, we generally refrain from treating edematous convexity, parasagittal, and parafalcine meningiomas in asymptomatic patients due to the relatively high risk of SRS-induced PTE.

Tumor Volume

Kollová et al. reported that the risk of post-SRS PTE reaches up to 30% in meningiomas that exceed 10 ml in volume, compared to only 10% in tumors smaller than 5 ml (15). Similarly, Han et al. found that large-volume meningiomas (>10 ml, median 15.2 ml) exhibited a 33.3% rate of symptomatic complications, even when treated with relatively low SRS doses (median dose of 12 Gy) (6). In a recent review, Islim et al. stated that SRS is not recommended for meningiomas with a volume that exceeds 10 ml (11). Based on these findings, our clinical practice does not employ single-fraction SRS for meningiomas larger than 10 ml. In our study, the median tumor volume was 3.3 ml, with the largest tumor measuring 10.2 ml.

Margin Dose

In studies reporting SRS-induced symptomatic PTE in over 10% of cases, the median margin doses ranged from 13.6 Gy to 18 Gy (7,8,15,19,27). Higher margin doses have been shown to significantly correlate with an increased risk of SRS-induced PTE (17). Based on this evidence, we opted for relatively lower doses, as inducing symptoms in asymptomatic patients with incidental meningiomas is undesirable. This low-dose strategy may have contributed to the low incidence of SRS-induced symptomatic PTE observed in our study, with the majority of our patients receiving a dose of 12 Gy. Although a dose of ≥13 Gy is generally considered effective for treating meningiomas, multiple studies have demonstrated that a dose of approximately 12 Gy is also sufficient for achieving long-term tumor control (10,15,28). Further, based on recent findings, Lee et al. recommended a margin dose of between 11 Gy and 14 Gy to achieve long-term local control in non-skull-base meningiomas. They also demonstrated that D98%—the dose received by 98% of the tumor volume—was a significant factor for local control, with a cutoff value of 11 Gy (16). In our study, the median tumor coverage was 99% (range, 98%–100%). Consequently, even for the meningiomas that received a margin dose of 11 Gy (n=4) in our study, tumor coverage was at least 98%, which is consistent with the recommendations of Lee et al. (16).

SRS-Induced Toxicity in Asymptomatic Meningiomas

Hoe et al. analyzed 320 asymptomatic meningioma patients treated with SRS. Approximately two-thirds of the meningiomas were located in the hemispheric regions, while the remainder were skull-base meningiomas. In their study, 5.9% of patients exhibited pretreatment PTE. Following SRS (with a median dose of 13 Gy), 15.3% of patients developed new or increased PTE, 8.8% became symptomatic, and 1.3% experienced persistent neurological symptoms. Large tumor volumes (>4.2 cc), hemispheric tumor locations, and the presence of pretreatment PTE were associated with an increased risk of post-SRS PTE (8).

In the recent multicenter IMPASSE study, which included both skull-base and non-skull-base asymptomatic meningiomas, new neurologic deficits were reported in 2.3% of patients treated with SRS, while excellent local tumor control was achieved (99% over a mean follow-up of 57.2 months). The mean margin dose was 12.9 Gy (26). Our toxicity outcomes were comparable to those of the IMPASSE study, with 1.9% of our patients developing neurologic deficits due to SRS-induced PTE.

SRS vs. Surgery

If therapeutic intervention is considered for a non-skull-base asymptomatic meningioma, surgical resection is preferable over SRS when the tumor volume exceeds 10 ml (4); this may also be a more appropriate option in the presence of PTE (3,8,17,29). Additionally, surgery may be considered even for SRS-eligible tumors, such as those included in this study—particularly when located in the convexity, parasagittal, or parafalcine locations—as surgery can achieve high rates of complete resection with low permanent morbidity (25). Moreover, a key advantage of surgery is the ability to establish a pathological diagnosis, which is critical for detecting higher-grade tumors. However, it is well established that the vast majority of incidental meningiomas (94%) are WHO grade 1, while grade 3 tumors account for less than 1% (12). Notably, the IMPASSE trial revealed that only 1% of patients with asymptomatic meningiomas progressed after SRS, despite the absence of histological confirmation (9). Furthermore, one of the most significant advantages of SRS compared to surgery is its minimally invasive nature—frame-based Gamma Knife radiosurgery requires only local anesthesia, while mask-based SRS is a completely non-invasive procedure. Importantly, SRS does not appear to increase the risk of malignant transformation in meningiomas compared to surgery alone (19).

Limitations

The main limitations of this study include its retrospective design, its single-institution setting, and the small number of SRS-induced PTE cases (n=3), all of which may limit the generalizability of the results. Additionally, it is possible that the relatively small sample size (n=52) limited the statistical power to detect more subtle associations. Consequently, we were unable to demonstrate an association between SRS-induced PTE and factors such as tumor volume and margin dose, which have been well established as predictors of SRS-induced PTE in previous studies. Moreover, in our cohort, 75% of patients received a margin dose of 12 Gy, 17.3% received 13 Gy, and only 7.7% (n=4) received 11 Gy. The limited variability in margin doses (11 Gy–13 Gy) possibly constrained our ability to identify dose-related effects. In addition, we were unable to evaluate the effects of pre-existing PTE on the development of SRS-induced PTE, as asymptomatic patients with pre-existing PTE were not included in this study due to our clinical policy of avoiding SRS in such cases.

CONCLUSION

Considering that no SRS-induced PTE was observed among patients below 65 years of age, our findings suggest that SRS, when administered with a median margin dose of 12 Gy (range: 11 Gy–13 Gy), may be a safe treatment modality in terms of PTE risk for this population, with asymptomatic convexity, parasagittal, or parafalcine meningiomas without pre-existing PTE. However, elderly patients with asymptomatic parasagittal or parafalcine meningiomas may be at an in-

creased risk of developing SRS-induced PTE. Therefore, the decision to treat such patients with SRS should be made cautiously, taking into account the potential risk of complications; moreover, the safety profile of SRS should be further validated in studies with larger patient populations.

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Declarations

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Availability of data and materials: The datasets generated and/or analyzed during the current study are available from the corresponding author by reasonable request.

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AUTHORSHIP CONTRIBUTION

Study conception and design: OBC, MR, BDI, AA
Data collection: OBC, SZ, AY, DC, OA
Analysis and interpretation of results: OBC, MR
Draft manuscript preparation: OBC
Critical revision of the article: OBC, MR, BDI
Other (study supervision, fundings, materials, etc...): AY, AA, OBC
All authors (OBC, MR, BDI, OA, SZ, AY, DC, AA) reviewed the results and approved the final version of the manuscript.

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